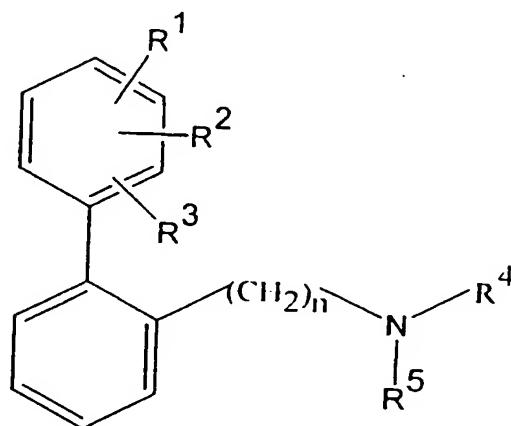


Patent claims:

1. A substituted 2-dialkylaminoalkylbiphenyl compound of formula I



I,

wherein

n is 1 or 2;

R¹, R², R³, which are identical or different, represent H, F, Cl, Br, CN, NO₂, CHO, SO₂CH₃, SO₂CF₃, OR⁶, NR⁶R⁷, a C₁₋₆-alkyl, an aryl, an acetyl, an acetamidyl or a benzoyl group or represent an aryl group bonded via a C₁₋₆-alkylene group;

or R¹ and R² together denote the group OCH₂O, OCH₂CH₂O, CH=CHO, CH=C(CH₃)O or CH=CHNH;

R⁴, R⁵, which are identical or different, represent H, or a C₁₋₆-alkyl group;

R⁶, R⁷, which are identical or different, represent H, a C₁₋₆-alkyl or an aryl group, or represent an aryl group bonded via a C₁₋₆-alkylene group;

or a physiologically tolerated salt,

provided that the compounds:

2'-dimethylaminomethylbiphenyl-2-carbaldehyde;

biphenyl-2-ylmethyldimethylamine;

2'-dimethylaminomethylbiphenyl-2-ol, and the corresponding hydrochloride;

(2',3'-dimethoxybiphenyl-2-ylmethyl)dimethylamine, and the corresponding hydrochloride and hydrobromide;

(4'-methylbiphenyl-2-ylmethyl)-dimethylamine;

(2'-methylbiphenyl-2-ylmethyl)-dimethylamine;

4-chloro-2'-dimethylaminomethylbiphenyl-2-carbonitrile;

(2'-dimethylaminomethylbiphenyl-2-yl)methanol;

2'-dimethylaminomethylbiphenyl-2,3-diol, and the corresponding hydrobromide;

[2-(3',4'-dimethoxybiphenyl-2-yl)ethyl]-dimethylamine, and the corresponding hydrochloride;

[2-(2',3'-dimethoxy-6'-methylbiphenyl-2-yl)ethyl]-dimethylamine, and the corresponding hydrobromide;

and

biphenyl-2-ylethyldimethylamine are excluded.

2. A substituted 2-dialkylaminoalkylbiphenyl compound according to claim 1, wherein one or more of R¹, R² and R³ represent a C₁₋₃-alkyl group.

3. A substituted 2-dialkylaminoalkylbiphenyl compound according to claim 1, wherein one or more of R¹, R² and R³ represent an aryl group bonded via a C₁₋₃-alkylene group.

4. A substituted 2-dialkylaminoalkylbiphenyl compound according to claim 1, wherein R⁴ or R⁵, or both, represent a C₁₋₃-alkyl group.

5. A substituted 2-dialkylaminoalkylbiphenyl compound according to claim 1, wherein R⁶ or R⁷, or both, represent a C₁₋₃-alkyl group.

6. A substituted 2-dialkylaminoalkylbiphenyl compound according to claim 1, wherein R⁶ or R⁷, or both, represent an aryl group bonded via a C₁₋₃-alkylene group.

7. A substituted 2-dialkylaminoalkylbiphenyl compound according to claim 1, selected from the group consisting of:

(3'-methoxybiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(4'-chlorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

2'-dimethylaminomethylbiphenyl-3-ol and the corresponding hydrochloride;

(2'-methoxybiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(3'-chlorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(2'-fluorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(3'-fluorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(4'-fluorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(3'-chloro-4'-fluorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(3'-methoxybiphenyl-2-ylethyl)dimethylamine and the corresponding hydrochloride;

dimethyl-[2-(2-methylbenzofuran-4-yl)benzyl]amine and the corresponding hydrochloride;

2'-dimethylaminomethylbiphenyl-2-carbaldehyde hydrochloride;

(3'-difluoromethylbiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

2'-dimethylaminomethylbiphenyl-3-carbaldehyde and the corresponding hydrochloride;

biphenyl-2-ylmethyldimethylamine hydrochloride;

(3',4'-dichlorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(3',5'-dichlorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

dimethyl-(4'-nitro-3'-trifluoromethylbiphenyl-2-ylmethyl)-amine and the corresponding hydrochloride;

(3',4'-difluorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(4'-fluoro-3'-trifluoromethylbiphenyl-2-ylmethyl)dimethyl-amine and the corresponding hydrochloride;

(4'-chloro-3'-methoxybiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

N-(2'-dimethylaminomethyl-3-trifluoromethoxybiphenyl-4-yl)acetamide and the corresponding hydrochloride;

(3'-isopropoxybiphenyl-2-ylmethyl)dimethylamine and the corresponding and the corresponding hydrochloride;

2'-(2-dimethylaminoethyl)biphenyl-3-ol and the corresponding hydrochloride;

4-chloro-2'-dimethylaminomethylbiphenyl-3-ol and the corresponding hydrochloride;

[2-(1*H*-indol-5-yl)benzyl]dimethylamine and the corresponding hydrochloride;

(4'-methanesulfonylbiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(2',4'-dichlorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(2',3'-difluorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(2',5'-difluorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

(2-benzo[1,3]dioxol-5-ylbenzyl)dimethylamine and the corresponding hydrochloride;

1-[2'-(2-dimethylaminoethyl)biphenyl-3-yl]ethanone and the corresponding hydrochloride;

[2-(3'-isopropoxybiphenyl-2-yl)ethyl]dimethylamine and the corresponding hydrochloride;

[2-(4'-chloro-3'-methoxybiphenyl-2-yl)ethyl]dimethylamine and the corresponding hydrochloride;

4-chloro-2'-(2-dimethylaminoethyl)biphenyl-3-ol and the corresponding hydrochloride;

dimethyl-(3'-nitrobiphenyl-2-ylmethyl)amine and the corresponding hydrochloride;

4-amino-2'-dimethylaminomethylbiphenyl-3-ol and the corresponding dihydrochloride;

(3',5'-difluorobiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

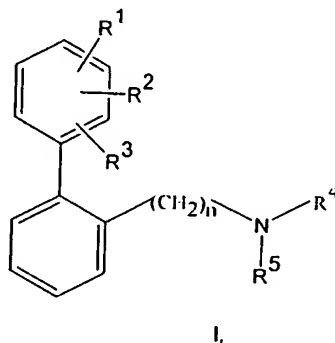
(2',5'-dimethoxybiphenyl-2-ylmethyl)dimethylamine and the corresponding hydrochloride;

2'-dimethylaminomethyl-5-trifluoromethoxybiphenyl-2-ylamine and the corresponding dihydrochloride;

N-(2'-dimethylaminomethyl-5-trifluoromethoxybiphenyl-2-yl)acetamide and the corresponding hydrochloride; and

3,5-dichloro-2'-dimethylaminomethyl-biphenyl-4-ylamine and the corresponding hydrochloride.

8. A process for the preparation of a substituted 2-dimethylaminoalkylbiphenyl compound of formula I,



wherein

n is 1 or 2;

R¹, R², R³, which are identical or different, represent H, F, Cl, Br, CN, NO₂, CHO, SO₂CH₃, SO₂CF₃, OR⁶, NR⁶R⁷, a C₁₋₆-alkyl, an aryl, an acetyl, an acetamidyl or a benzoyl group or represent an aryl group bonded via a C₁₋₆-alkylene group;

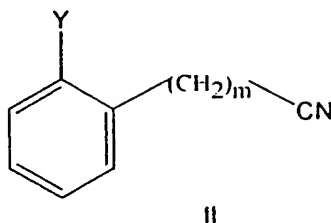
or R¹ and R² together denote the group OCH₂O, OCH₂CH₂O, CH=CHO, CH=C(CH₃)O or CH=CHNH₂;

R⁴, R⁵, which are identical or different, represent H, or a C₁₋₆-alkyl group; and

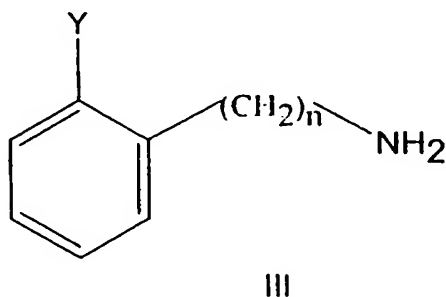
R⁶, R⁷, which are identical or different, represent H, a C₁₋₆-alkyl or an aryl group, or represent an aryl group bonded via a C₁₋₆-alkylene group;

the process comprising:

(a) reducing a compound of formula II



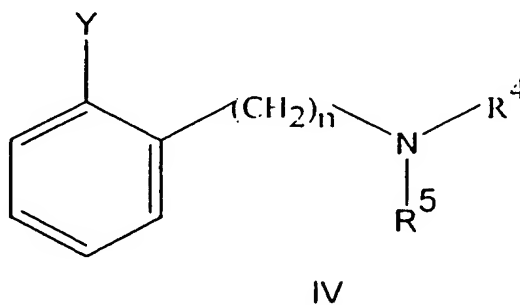
wherein Y denotes Cl, Br or I and m denotes 0 or 1, in solution with a first reducing agent to give rise to a compound of formula III,



wherein n denotes 1 or 2,

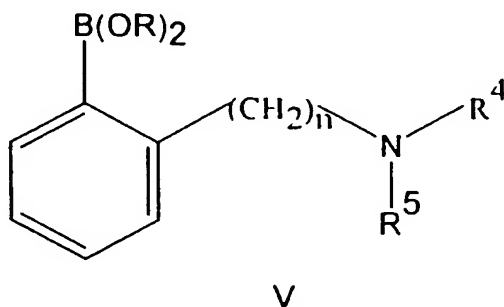
which is purified and isolated;

(b) reacting a compound of formula III with an aliphatic C₁₋₆-aldehyde in the presence of a second reducing agent to give rise to a compound of the general formula IV



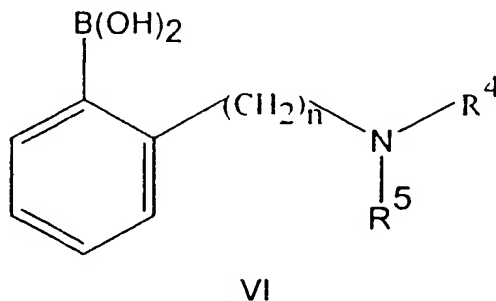
wherein R⁴ and R⁵ have the meaning according to formula I, which compound of formula IV is purified and isolated;

(c) converting a compound of formula IV by halogen-metal exchange and subsequent reaction with a boric acid ester at a temperature of $\leq 0^{\circ}\text{C}$ to give rise to a compound of formula V,



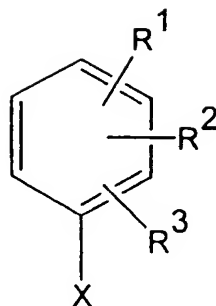
wherein R denotes an alkyl group;

(d) reacting a compound of formula V with an aqueous acid to give rise to a compound of formula VI



which is purified and isolated; and

(e) reacting a compound of formula V or VI in a transition metal-catalysed reaction in an aliphatic ether, a hydrocarbon, an alcohol, a chlorinated hydrocarbon, water or mixtures thereof at a temperature between 20 and 150°C with a compound of formula VII



VII,

wherein X denotes Cl, Br, I or OSO₂C_pF_(2p+1) and R¹, R², R³, which are identical or different, represent H, F, Cl, Br, CN, NO₂, CHO, SO₂CH₃, SO₂CF₃, OR⁶, NR⁶R⁷, a C₁₋₆-alkyl, an aryl, an acetyl, an acetamidyl or a benzoyl group or represent an aryl group bonded via a C₁₋₆-alkylene group, to give rise to a compound of formula I, which is purified and isolated.

9. A process according to claim 8, wherein the compound of formula II is reduced with lithium aluminium hydride or diisobutylaluminium hydride, or both.

10. A process according to claim 8, wherein the compound of formula III is reacted with aliphatic C₁₋₆-aldehydes in the presence of formic acid, or sodium borohydride, or both.

11. A process according to claim 8, wherein the halogen-metal exchange is carried out with magnesium or butyllithium, or both.

12. A process according to claim 8, wherein the boric acid ester is a trialkyl borate.

13. The process of Claim 12, wherein the trialkyl borate is trimethyl borate.

14. A process according to claim 8, wherein a compound of formula V is reacted with hydrochloric acid to give rise to a compound of formula VI.

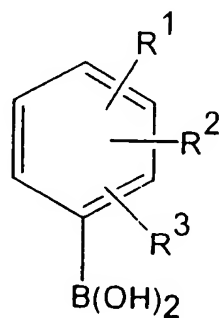
15. A process according to claim 8, wherein a compound of formula V or VI is reacted in a reaction catalysed by palladium(0) compounds, or palladium(II) salts, or both.

16. A process according to claim 8, wherein the transition metal-catalysed reaction is carried out in 1,4-dioxane, tetrahydrofuran, toluene, hexane, ethanol, isopropanol, chloroform, methylene chloride, water or a mixture thereof.

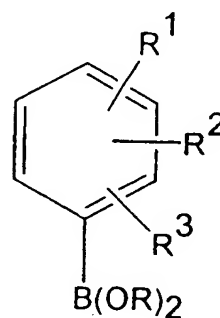
17. The process of Claim 8, wherein the compound of the general formula V in step (c) is optionally isolated and purified prior to reacting with an aqueous acid in step (d).

18. The process of Claim 15, wherein the reaction is catalyzed by tetrakis(triphenylphosphine)palladium, bis(dibenzylideneacetone)palladium, elemental palladium on active charcoal, palladium(II) chloride or palladium(II) acetate, or mixtures thereof.

19. A method for preparing a substituted 2-dimethylaminoalkylbiphenyl derivative of the general formula I according to claim 1, comprising reacting a compound of the general formula VIII or IX



VIII



IX,

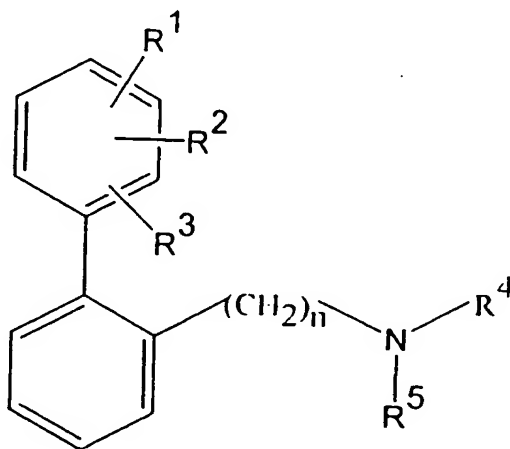
wherein R¹ to R³ have the meaning according to the general formula I according to claim 1, in a transition metal-catalysed reaction in an aliphatic ether, a hydrocarbon, an alcohol, a chlorinated hydrocarbon, water or mixtures

thereof at a temperature between 20 and 150°C with a compound of the general formula III or IV to give rise to a compound of the general formula I, which is purified and isolated.

20. A process according to claim 19, wherein a compound formula VIII or IX is reacted in a reaction catalysed by palladium(0) compounds or by palladium(II) salts, or both.

21. The process of Claim 20, wherein the reaction is catalyzed by tetrakis(triphenylphosphine)palladium, bis(dibenzylideneacetone)palladium, elemental palladium on active charcoal, palladium(II) chloride or palladium(II) acetate, or mixtures thereof.

22. A pharmaceutical composition comprising, a substituted 2-dialkylaminoalkylbiphenyl compound of formula I



I,

wherein

n is 1 or 2;

R¹, R², R³, which are identical or different, represent H, F, Cl, Br, CN, NO₂, CHO, SO₂CH₃, SO₂CF₃, OR⁶, NR⁶R⁷, a C₁₋₆-alkyl, an aryl, an acetyl, an acetamidyl or a benzoyl group or represent an aryl group bonded via a C₁₋₆-alkylene group;

or R¹ and R² together denote the group OCH₂O, OCH₂CH₂O, CH=CHO, CH=C(CH₃)O or CH=CHNH;

R⁴, R⁵, which are identical or different, represent H, or a C₁₋₆-alkyl group;

R⁶, R⁷, which are identical or different, represent H, a C₁₋₆-alkyl or an aryl group, or represent an aryl group bonded via a C₁₋₆-alkylene group;

With the proviso that the compounds:

2'-dimethylaminomethylbiphenyl-2-carbaldehyde;

biphenyl-2-ylmethyldimethylamine;

2'-dimethylaminomethylbiphenyl-2-ol, and the corresponding hydrochloride;

(2',3'-dimethoxybiphenyl-2-ylmethyl)dimethylamine, and the corresponding hydrochloride and hydrobromide;

(4'-methylbiphenyl-2-ylmethyl)-dimethylamine;

(2'-methylbiphenyl-2-ylmethyl)-dimethylamine;

4-chloro-2'-dimethylaminomethylbiphenyl-2-carbonitrile;

(2'-dimethylaminomethylbiphenyl-2-yl)methanol;

2'-dimethylaminomethylbiphenyl-2,3-diol, and the corresponding hydrobromide;

[2-(3',4'-dimethoxybiphenyl-2-yl)ethyl]-dimethylamine, and the corresponding hydrochloride;

[2-(2',3'-dimethoxy-6'-methylbiphenyl-2-yl)ethyl]-dimethylamine, and the corresponding hydrobromide;

and

biphenyl-2-ylethyldimethylamine are excluded,
and a pharmaceutically acceptable excipient.

23. A method for the treatment of pain, inflammatory and allergic reactions, depressions, drug and alcohol abuse, gastritis, diarrhoea, urinary incontinence, cardiovascular diseases, respiratory tract diseases, coughing, mental illnesses or epilepsy, comprising administering a pharmaceutically effective amount of a pharmaceutical composition of claim 22 to a patient in need thereof.

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